Schmidt
827255

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=> dis his

     (FILE 'HOME' ENTERED AT 13:10:59 ON 31 AUG 2001)

     FILE 'CAPLUS' ENTERED AT 13:11:27 ON 31 AUG 2001

=> e therapeutic agent/ct 5
E#   FREQUENCY     AT      TERM
--   ---------     --      ----
E1           5      2      THERALITES/CT
E2           0      1      THERAPEUTIC/CT
E3           0        --> THERAPEUTIC AGENT/CT
E4           0      2      THERAPEUTIC AGENTS/CT
E5           0      2      THERAPEUTIC AGENTS, MYOCARDIAL INFARCTION/CT

=> e e4+all/ct
E1           0    -->  Therapeutic agents/CT
E2        8249      USE  Drugs/CT
********* END***

=> e asialoglycoprotein receptor/ct 5
E#   FREQUENCY     AT      TERM
--   ---------     --      ----
E1           0      3      ASIALOGANGLIOSIDES/CT
E2           0      1      ASIALOGLYCOPROTEIN/CT
E3           0        --> ASIALOGLYCOPROTEIN RECEPTOR/CT
E4         196     22      ASIALOGLYCOPROTEIN RECEPTORS/CT
E5           0      1      ASIALOGLYCOPROTEIN-BINDING/CT

=> e e4+all/ct
E1         331   BT4  Proteins, general/CT
E2      177763     BT3  Proteins, specific or class/CT
E3      225079       BT2  Receptors/CT
E4        1966         BT1  Protein receptors/CT
E5         196           -->  Asialoglycoprotein receptors/CT
                           HN   Valid heading during volume 126 (1997) to
                                present.
E6                         OLD  Proteins (L) asialoglycoprotein-binding/CT
E7                         OLD  Proteins, specific or class (L)
                                asialoglycoprotein-binding/CT
E8                         OLD  Proteins, specific or class (L)
                                asialoglycoprotein-binding, H1/CT
E9                         OLD  Proteins, specific or class (L)
                                asialoglycoprotein-binding, H2/CT
E10                        OLD  Receptors (L) asialoglycoprotein/CT
E11                        OLD  Sialoglycoprotein receptors (L)
                                asialosialoglycoprotein/CT
E12                        UF   Asialoglycoprotein-binding glycoproteins/CT
E13                        UF   Asialoglycoprotein-binding proteins/CT
E14                        UF   Asialoprotein receptors/CT
E15                        UF   Galactose receptors/CT
E16                        UF   Glucoproteins (L)
asialoglycoprotein-binding/CT
E17                        UF   Glycoproteins (L)
asialoglycoprotein-binding/CT
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Prepared by M. Hale 308-4258

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E18                                  UF   Glycoproteins, specific or class (L)
                                          asialoglycoprotein-binding/CT
E19                                  UF   Proteins (L) asialoglycoprotein receptor/CT
E20                                  UF   Receptors, galactose/CT
E21                                  UF   Sialoglycoproteins (L) asialo-, receptors/CT
E22        35498                     RT   Glycoproteins, specific or class/CT
*********  END***

=> s e5-22
           196 "ASIALOGLYCOPROTEIN RECEPTORS"/CT
        456770 PROTEINS/CT
           755 ASIALOGLYCOPROTEIN/IT
           300 ASIALOGLYCOPROTEINS/IT
           860 ASIALOGLYCOPROTEIN/IT
                 ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
        304786 BINDING/IT
           109 BINDINGS/IT
        304845 BINDING/IT
                 ((BINDING OR BINDINGS)/IT)
            30 "PROTEINS (L) ASIALOGLYCOPROTEIN-BINDING"/CT
        177763 "PROTEINS, SPECIFIC OR CLASS"/CT
           755 ASIALOGLYCOPROTEIN/IT
           300 ASIALOGLYCOPROTEINS/IT
           860 ASIALOGLYCOPROTEIN/IT
                 ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
        304786 BINDING/IT
           109 BINDINGS/IT
        304845 BINDING/IT
                 ((BINDING OR BINDINGS)/IT)
            17 "PROTEINS, SPECIFIC OR CLASS (L) ASIALOGLYCOPROTEIN-BINDING"/CT
        177763 "PROTEINS, SPECIFIC OR CLASS"/CT
           755 ASIALOGLYCOPROTEIN/IT
           300 ASIALOGLYCOPROTEINS/IT
           860 ASIALOGLYCOPROTEIN/IT
                 ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
        304786 BINDING/IT
           109 BINDINGS/IT
        304845 BINDING/IT
                 ((BINDING OR BINDINGS)/IT)
          6881 H1/IT
             5 "PROTEINS, SPECIFIC OR CLASS (L) ASIALOGLYCOPROTEIN-BINDING,
               H1"/CT
        177763 "PROTEINS, SPECIFIC OR CLASS"/CT
           755 ASIALOGLYCOPROTEIN/IT
           300 ASIALOGLYCOPROTEINS/IT
           860 ASIALOGLYCOPROTEIN/IT
                 ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
        304786 BINDING/IT
           109 BINDINGS/IT
        304845 BINDING/IT
                 ((BINDING OR BINDINGS)/IT)
         10613 H2/IT
             2 "PROTEINS, SPECIFIC OR CLASS (L) ASIALOGLYCOPROTEIN-BINDING,
               H2"/CT
        225079 RECEPTORS/CT
```

```
   755 ASIALOGLYCOPROTEIN/IT
   300 ASIALOGLYCOPROTEINS/IT
   860 ASIALOGLYCOPROTEIN/IT
         ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
   495 "RECEPTORS (L) ASIALOGLYCOPROTEIN"/CT
   129 SIALOGLYCOPROTEIN RECEPTORS/CT
   115 ASIALOSIALOGLYCOPROTEIN/IT
   115 "SIALOGLYCOPROTEIN RECEPTORS (L) ASIALOSIALOGLYCOPROTEIN"/CT
     0 "ASIALOGLYCOPROTEIN-BINDING GLYCOPROTEINS"/CT
     0 "ASIALOGLYCOPROTEIN-BINDING PROTEINS"/CT
     0 "ASIALOPROTEIN RECEPTORS"/CT
     0 "GALACTOSE RECEPTORS"/CT
     0 GLUCOPROTEINS/CT
   755 ASIALOGLYCOPROTEIN/IT
   300 ASIALOGLYCOPROTEINS/IT
   860 ASIALOGLYCOPROTEIN/IT
         ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
304786 BINDING/IT
   109 BINDINGS/IT
304845 BINDING/IT
         ((BINDING OR BINDINGS)/IT)
     0 "GLUCOPROTEINS (L) ASIALOGLYCOPROTEIN-BINDING"/CT
 60241 GLYCOPROTEINS/CT
   755 ASIALOGLYCOPROTEIN/IT
   300 ASIALOGLYCOPROTEINS/IT
   860 ASIALOGLYCOPROTEIN/IT
         ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
304786 BINDING/IT
   109 BINDINGS/IT
304845 BINDING/IT
         ((BINDING OR BINDINGS)/IT)
     4 "GLYCOPROTEINS (L) ASIALOGLYCOPROTEIN-BINDING"/CT
 35498 "GLYCOPROTEINS, SPECIFIC OR CLASS"/CT
   755 ASIALOGLYCOPROTEIN/IT
   300 ASIALOGLYCOPROTEINS/IT
   860 ASIALOGLYCOPROTEIN/IT
         ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
304786 BINDING/IT
   109 BINDINGS/IT
304845 BINDING/IT
         ((BINDING OR BINDINGS)/IT)
     2 "GLYCOPROTEINS, SPECIFIC OR CLASS (L)
ASIALOGLYCOPROTEIN-BINDING
       "/CT
456770 PROTEINS/CT
   755 ASIALOGLYCOPROTEIN/IT
   300 ASIALOGLYCOPROTEINS/IT
   860 ASIALOGLYCOPROTEIN/IT
         ((ASIALOGLYCOPROTEIN OR ASIALOGLYCOPROTEINS)/IT)
202205 RECEPTOR/IT
330579 RECEPTORS/IT
366576 RECEPTOR/IT
         ((RECEPTOR OR RECEPTORS)/IT)
    15 "PROTEINS (L) ASIALOGLYCOPROTEIN RECEPTOR"/CT
     0 "RECEPTORS, GALACTOSE"/CT
```

```
          8087 SIALOGLYCOPROTEINS/CT
          1587 ASIALO/IT
        330579 RECEPTORS/IT
           144 "SIALOGLYCOPROTEINS (L) ASIALO-, RECEPTORS"/CT
         35498 "GLYCOPROTEINS, SPECIFIC OR CLASS"/CT
L1       36179 ("ASIALOGLYCOPROTEIN RECEPTORS"/CT OR "PROTEINS (L)
ASIALOGLYCOP
               ROTEIN-BINDING"/CT OR "PROTEINS, SPECIFIC OR CLASS (L)
ASIALOGLY
               COPROTEIN-BINDING"/CT OR "PROTEINS, SPECIFIC OR CLASS (L)
ASIALO
               GLYCOPROTEIN-BINDING, H1"/CT OR "PROTEINS, SPECIFIC OR CLASS
               (L) ASIALOGLYCOPROTEIN-BINDING, H2"/CT OR "RECEPTORS (L)
ASIALOG
               LYCOPROTEIN"/CT OR "SIALOGLYCOPROTEIN RECEPTORS (L)
ASIALOSIALOG
               LYCOPROTEIN"/CT OR "ASIALOGLYCOPROTEIN-BINDING
GLYCOPROTEINS"/CT
                OR "ASIALOGLYCOPROTEIN-BINDING PROTEINS"/CT OR "ASIALOPROTEIN
               RECEPTORS"/CT OR "GALACTOSE RECEPTORS"/CT OR "GLUCOPROTEINS
(L)
               ASIALOGLYCOPROTEIN-BINDING"/CT OR "GLYCOPROTEINS (L)
ASIALOGLYCO
               PROTEIN-BINDING"/CT OR "GLYCOPROTEINS, SPECIFIC OR CLASS (L)
               ASIALOGLYCOPROTEIN-BINDING"/CT OR "PROTEINS (L)
ASIALOGLYCOPROTE
               IN RECEPTOR"/CT OR "RECEPTORS, GALACTOSE"/CT OR
"SIALOGLYCOPROTE
               INS (L) ASIALO-, RECEPTORS"/CT OR "GLYCOPROTEINS, SPECIFIC OR
               CLASS"/CT)

=> e desialyated glycoprotein alpha 1/ct
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     1     DESIALATED/CT
E2           0     2     DESIALATED .ALPHA.1-ACID GLYCOPROTEINS/CT
E3           0       --> DESIALYATED GLYCOPROTEIN ALPHA 1/CT
E4           0     1     DESIALYLATED/CT
E5           0     2     DESIALYLATED FETUINS/CT
E6           0     2     DESIALYLATED TRANSFERRINS/CT
E7           0     2     DESIALYLATION/CT
E8           0     8     DESIANTHA/CT
E9           1     7     DESIANTHA CAUDATA/CT
E10          1     7     DESIANTHA DIVERSIPES/CT
E11          0     1     DESICATA/CT
E12          0     1     DESICCANT/CT

=> e e2+all/ct
E1           0   -->  Desialated .alpha.1-acid glycoproteins/CT
E2                  USE  .alpha.1-Acid glycoprotein (L) asialo-.alpha.1-acid/CT
*********  END***

=> s e2
          581 .ALPHA.1-ACID GLYCOPROTEIN/CT
         1587 ASIALO/IT
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Prepared by M. Hale 308-4258

```
          376893 ALPHA/IT
              22 ALPHAS/IT
          376898 ALPHA/IT
                   ((ALPHA OR ALPHAS)/IT)
          920768 1/IT
         1521827 ACID/IT
          758047 ACIDS/IT
         1976555 ACID/IT
                   ((ACID OR ACIDS)/IT)
L2            53 ".ALPHA.1-ACID GLYCOPROTEIN (L) ASIALO-.ALPHA.1-ACID"/CT

=> e target delivery/ct 5
E#   FREQUENCY     AT      TERM
--   ---------     --      ----
E1           0      1      TARENTULA/CT
E2           0      1      TARGET/CT
E3           0        --> TARGET DELIVERY/CT
E4           0      2      TARGET OF ANTIPROLIFERATIVE ANTIBODY PROTEINS, 1/CT
E5           0      1      TARGETED/CT

=> e delivery/ct 5
E#   FREQUENCY     AT      TERM
--   ---------     --      ----
E1           2      6      DELITSCHIA CONFERTASPORA/CT
E2           1             DELITSCHIA WINTERI/CT
E3           0      1 --> DELIVERY/CT
E4           0      2      DELIVERY APP./CT
E5           0      2      DELIVERY APP., FEEDERS/CT

=> e
E6         149      2      DELIVERY APPARATUS/CT
E7           0      2      DELIVERY APPARATUS (L) DISPENSING/CT
E8           0      2      DELIVERY APPARATUS (L) DISTRIBUTING/CT
E9           0      2      DELIVERY APPARATUS (L) FEEDERS/CT
E10          0      2      DELIVERY APPARATUS (L) MICROPIPETS/CT
E11          0      2      DELIVERY APPARATUS (L) PIPETS/CT
E12          0      2      DELIVERY SYSTEMS (AGROCHEMICAL)/CT
E13          0      2      DELIVERY SYSTEMS (PHARMACEUTICAL)/CT
E14          0      2      DELIVERY SYSTEMS, AGROCHEM./CT
E15          0      1      DELLA-CELLAE/CT
E16          0      1      DELLECHIAJEI/CT
E17          2      2      DELLENITE/CT

=> e e13+all/ct
E1           0    -->  Delivery systems (pharmaceutical)/CT
E2       32058      USE  Drug delivery systems/CT
*********  END***

=> s e3
'E3' NOT FOUND
The E# entered is not currently defined.

=> s e2
L3       32058 "DRUG DELIVERY SYSTEMS"/CT
```

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=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        73.44      73.59

FILE 'REGISTRY' ENTERED AT 13:15:00 ON 31 AUG 2001
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STRUCTURE FILE UPDATES:   30 AUG 2001  HIGHEST RN 354111-05-0
DICTIONARY FILE UPDATES:  30 AUG 2001  HIGHEST RN 354111-05-0

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> s (doxorubicin or vincristine or daunorubicin or amphiphatic amine)/cn
             1 DOXORUBICIN/CN
             1 VINCRISTINE/CN
             1 DAUNORUBICIN/CN
             0 AMPHIPHATIC AMINE/CN
L4           3 (DOXORUBICIN OR VINCRISTINE OR DAUNORUBICIN OR AMPHIPHATIC
AMINE
               )/CN

=> e avidin biotin/cn 5
E1           1     AVIDIN (CHICKEN CLONE .LAMBDA.CAV4 PROTEIN MOIETY
REDUCED)/C
                   N
E2           1     AVIDIN (CHICKEN CLONE 44 GENE AVD PRECURSOR)/CN
E3           0 --> AVIDIN BIOTIN/CN
E4           1     AVIDIN-RELATED PROTEIN 1 (CHICKEN CLONE PGAV1.8 GENE AVR1
PR
                   ECURSOR)/CN
E5           1     AVIDIN-RELATED PROTEIN 2 (CHICKEN CLONE PGAV3.7 GENE AVR2
PR
                   ECURSOR)/CN

=> e "avidin-biotin"/cn
E1           1     AVIDIN (CHICKEN CLONE .LAMBDA.CAV4 PROTEIN MOIETY
REDUCED)/C
                   N
E2           1     AVIDIN (CHICKEN CLONE 44 GENE AVD PRECURSOR)/CN
E3           0 --> AVIDIN-BIOTIN/CN
E4           1     AVIDIN-RELATED PROTEIN 1 (CHICKEN CLONE PGAV1.8 GENE AVR1
PR
                   ECURSOR)/CN
E5           1     AVIDIN-RELATED PROTEIN 2 (CHICKEN CLONE PGAV3.7 GENE AVR2
PR
                   ECURSOR)/CN
```

```
E6              1     AVIDIN-RELATED PROTEIN 3 (CHICKEN CLONE PGAV3.3 GENE AVR3
PR
                      ECURSOR)/CN
E7              1     AVIDIN-RELATED PROTEIN 4/53 (CHICKEN CLONE
PGAV2H48/PGAV2H52
                       GENE AVR4/5 PRECURSOR)/CN
E8              1     AVIDINORUBICIN/CN
E9              1     AVIDINS/CN
E10             1     AVIDINS, D, EGG WHITE/CN
E11             1     AVIDINS, DH, EGG WHITE/CN
E12             1     AVIGEL 108/CN

=> e thiol maleamide/cn 5
E1              1     THIOL GROUP-TERMINATED NEOPRENE RUBBER/CN
E2              1     THIOL GROUP-TERMINATED SYNTHETIC RUBBER/CN
E3              0 --> THIOL MALEAMIDE/CN
E4              1     THIOL METHYLTRANSFERASE/CN
E5              1     THIOL OXIDASE/CN
```

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=> fil medl,caplus,biosis,embase,wpids,jicst
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               15.82      89.41

FILE 'MEDLINE' ENTERED AT 13:16:26 ON 31 AUG 2001

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FILE 'EMBASE' ENTERED AT 13:16:26 ON 31 AUG 2001
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FILE 'WPIDS' ENTERED AT 13:16:26 ON 31 AUG 2001
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=> s (l3 or target? deliver? or drug deliver?) and (therap? agent? or
polynucleotide or cdna or protein or ribozyme or antisense dna or cytotoxic
or protein or doxorubicin or daunorubicin or amphiphat? amine or l4)
L5          1593 FILE MEDLINE
L6         11358 FILE CAPLUS
L7          3039 FILE BIOSIS
L8          3464 FILE EMBASE
L9           844 FILE WPIDS
L10          730 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L11        21028 (L3 OR TARGET? DELIVER? OR DRUG DELIVER?) AND (THERAP? AGENT?
```

```
              OR POLYNUCLEOTIDE OR CDNA OR PROTEIN OR RIBOZYME OR ANTISENSE
              DNA OR CYTOTOXIC OR PROTEIN OR DOXORUBICIN OR DAUNORUBICIN OR
              AMPHIPHAT? AMINE OR L4)

=> s (l1 or asialoglycoprotein? receptor? or l2 or desialyated glycoprotein?)
and l11
L12          11 FILE MEDLINE
L13         301 FILE CAPLUS
L14          19 FILE BIOSIS
L15          25 FILE EMBASE

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'
L16           5 FILE WPIDS
L17           3 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L18         364 (L1 OR ASIALOGLYCOPROTEIN? RECEPTOR? OR L2 OR DESIALYATED
GLYCOP
              ROTEIN?) AND L11

=> s l18 and (avidin(a)biotin or thiol(a)maleamide?)
L19           0 FILE MEDLINE
L20           2 FILE CAPLUS
L21           0 FILE BIOSIS
L22           0 FILE EMBASE
L23           0 FILE WPIDS
L24           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L25           2 L18 AND (AVIDIN(A) BIOTIN OR THIOL(A) MALEAMIDE?)

=> d 1-2 cbib abs

L25  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2001 ACS
1993:485515   Document No. 119:85515  Complete protection of antisense
     oligonucleotides against serum nuclease degradation by an avidin
     -biotin system.  Boado, Ruben J.; Pardridge, William M. (Sch.
     Med., UCLA, Los Angeles, CA, 90024, USA).  Bioconjugate Chem., 3(6),
     519-23 (English) 1992.  CODEN: BCCHES.  ISSN: 1043-1802.
AB   A complex of avidin, a cationic protein, and a monobiotinylated
     antisense oligonucleotide for the GLUT1 glucose transporter mRNA is taken
     up by cells in vitro and by organs in vivo via absorptive-mediated
```

endocytosis. In the present study, a GLUT1 biotinylated oligonucleotide-avidin construct showing complete protection against serum 3'-exonuclease-mediated degrdn. is described. 21-Mer antisense oligonucleotides complementary to nucleotides 162-182 and 161-181 of the bovine GLUT1 glucose transporter mRNA were synthesized with a 6-aminodeoxyuridine at positions 3 and 20, resp., biotinylated with NHS-biotin to yield near 5'- or near 3'-biotinylated oligonucleotide (bio-DNA), and 5'- or 3'-end radiolabeled. Serum induced a rapid degrdn. of unprotected (no avidin) [5'-32P]-5'-bio-DNA (>95% at 30 min). Avidin partially protected this construct (-31% of intact 21-mer oligo remained at 1 h). Similar results were obtained with the [3'-32P]-5'-bio-DNA; however, no degrdn. products of varying size were obsd., confirming that the degrdn. is mediated primarily by a 3'-exonuclease. Incubation of the [5'-32P]-3'-bio-DNA with serum showed a rapid conversion to the 20- and 19-mer forms (t1/2 .apprx. 13 min). Conversely, avidin totally protected this construct against the serum 3'-exonuclease. Avidin fully protects antisense oligonucleotides biotinylated at the near 3'-terminus against serum 3'-exonuclease degrdn., and this property may be useful for avidin-mediated **drug delivery** of oligonucleotides to tissues in vivo or to cultured cells in vitro.

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
1993:247616 Document No. 118:247616 **Drug delivery** of antisense oligonucleotides and peptides to tissues in vivo and to cells using **avidin-biotin** technology. Pardridge, William M.; Boado, Ruben J. (University of California, USA). PCT Int. Appl. WO 9222332 A2 19921223, 43 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US5085 19920617. PRIORITY: US 1991-716062 19910617.

AB A compn. is disclosed for delivery of an agent to cells in vitro or to tissues or organs in vivo. The compn. comprises avidin (or an avidin fusion **protein**) bound to a biotinylated agent to form an **avidin-biotin**-agent complex. A method is disclosed for delivery of an agent to cells using the **avidin-biotin** -agent complex. The complex is useful in diagnostic and therapeutic methods. Biotinylated peptide DDLVP (a vasopressin analog) was taken up by brain capillary prepns. when coupled to avidin, whereas minimal uptake was obsd. without the avidin transport vector. Uptake was mediated by the cationic nature of the avidin rather than the attached carbohydrate. Uptake of an avidin complex with a biotinylated antisense oligonucleotide (complementary to GLUT-1 glucose transporter mRNA) is also described. Further described are the protection by avidin of biotinylated antisense oligonucleotide against degrdn. by serum exonuclease and the facilitation of uptake of biotin by a cationized rat albumin-avidin conjugate.

=> s wong, j?/au,in or wong j?/au,in;s tsang, s?/au,in or tsang s?/au,in
'IN' IS NOT A VALID FIELD CODE
L26 1584 FILE MEDLINE
L27 1535 FILE CAPLUS
L28 2014 FILE BIOSIS

'IN' IS NOT A VALID FIELD CODE
L29 1523 FILE EMBASE
L30 354 FILE WPIDS
L31 22 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L32 7032 WONG, J?/AU,IN OR WONG J?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L33 109 FILE MEDLINE
L34 252 FILE CAPLUS
L35 197 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L36 106 FILE EMBASE
L37 26 FILE WPIDS
L38 4 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L39 694 TSANG, S?/AU,IN OR TSANG S?/AU,IN

=> s l32 and l39
L40 0 FILE MEDLINE
L41 0 FILE CAPLUS
L42 0 FILE BIOSIS
L43 0 FILE EMBASE
L44 0 FILE WPIDS
L45 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L46 0 L32 AND L39

=> s (l32 or l39) and l11
L47 0 FILE MEDLINE
L48 7 FILE CAPLUS
L49 1 FILE BIOSIS
L50 1 FILE EMBASE
L51 1 FILE WPIDS
L52 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L53 10 (L32 OR L39) AND L11

=> dup rem l53
PROCESSING COMPLETED FOR L53
L54 7 DUP REM L53 (3 DUPLICATES REMOVED)

=> d cbib abs 1-7

L54 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS
2001:294884 Document No. 134:300824 Use of virulence factors of pathogens to
improve liposomal delivery of **therapeutic agents**.
Cherwonogrodzky, John; **Wong, Jonathan P.**; Dininno, Vincent L.
(Canada, Minister of National Defence, Can.). U.S. US 6221386 B1

20010424, 8 pp., Cont.-in-part of U.S. Ser. No. 782,129, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1999-251304 19990217. PRIORITY: CA 1996-2171369 19960308; US 1997-782129 19970113.

AB Liposome-encapsulated antibiotic therapy has limited application against infectious organisms, which can sequester in non-phagocytic cells. Virulence factors of these infectious organisms, for example bacterial polysaccharides, when used in the formulation of liposomes can enhance the effectiveness of liposomes as delivery systems in the treatment of disease. In this manner, multi-functional liposomes can be developed to treat target diseases. In addn. to serving as antibiotic delivery systems, such liposomes also have an immunization effect. Thus, the liposomes can be used for both the prevention and treatment of diseases. For example, an 8.5% increase in uptake by Vero tissue culture of ciprofloxacin encapsulated in liposomes contg. Brucella abortus polysaccharides was obsd. compared to control. Uptake of liposomes with B. melitensis lipopolysaccharides (LPS) was comparable to std. liposomes, indicating that B. melitensis LPS did not affect the invasiveness of the liposomes in Vero tissue culture, nor did it prevent entry of liposomes into this tissue culture.

L54 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

2000:875156 Document No. 134:242526 Biodistribution characteristics of mannosylated, fucosylated, and galactosylated liposomes in mice. Kawakami, S.; **Wong, J.**; Sato, A.; Hattori, Y.; Yamashita, F.; Hashida, M. (Department of Drug Delivery Research, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan). Biochim. Biophys. Acta, 1524(2-3), 258-265 (English) 2000. CODEN: BBACAQ.

ISSN: 0006-3002. Publisher: Elsevier Science B.V..

AB The in vivo disposition behavior and pharmacokinetic characteristics of galactosylated (Gal), mannosylated (Man) and fucosylated (Fuc) liposomes were compared in this study. For the prepn. of the glycosylated liposomes, cholesten-5-yloxy-N-(4-((1-imino-2-.beta.-d-thiogalactosylethyl)amino)alkyl)formamide and its mannosylated and fucosylated derivs. (Man-C4-Chol and Fuc-C4-Chol, resp.) were synthesized.

The glycosylated liposomes are composed of distearoylphosphatidylcholine (DSPC), cholesterol (Chol), and Gal-C4-Chol (or Man-C4-Chol or Fuc-C4-Chol) with the molar ratio of 60:35:5. After i.v. injection in mice, these three types of [3H]cholesteryl hexadecyl ether-labeled glycosylated liposomes were rapidly eliminated from the circulating blood and preferentially recovered in the liver. In contrast, DSPC/Chol (60:40) liposomes without glycosylation were retained for a long time in the circulating blood. The uptake ratios by parenchymal cells (PC) and nonparenchymal cells (NPC) (PC/NPC ratios) for 0.5% Gal, Man and Fuc liposomes were found to be 15.1, 0.6 and 0.2, resp. The effect of predosing glycosylated **proteins** and liposomes on the hepatic uptake of 0.5% 3H-labeled Gal, Man, and Fuc liposomes was investigated and the results support the conclusion that Gal, Man, and Fuc liposomes are taken up by the liver via asialoglycoprotein receptors in PC, mannose receptors in NPC, and fucose receptors in NPC, resp. Interestingly, Gal liposomes were taken up by NPC rather than by PC at a high dose (5%).

Together with the finding that 5% Gal liposomes inhibit the hepatic uptake of 3H-labeled Fuc liposomes, this suggests that Gal-liposomes administered at a high dose will also be taken up by fucose receptors in NPC, that are considered to act as galactose particle receptors.

L54 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2001 ACS
1998:198231 Document No. 128:196663 Use of virulence factors of pathogens to improve liposomal delivery of antibiotics and/or vaccines. **Wong, Jonathan P.**; Dininno, Vincent L.; Cherwonogrodzky, John W. (Minister of National Defence, Can.). Can. Pat. Appl. CA 2171369 AA 19970909, 21 pp. (English). CODEN: CPXXEB. APPLICATION: CA 1996-2171369 19960308.

AB Liposome encapsulated antibiotic therapy has limited application against infectious organisms which can sequester in non-phagocytic cells. Virulence factors of these infectious organisms, for example bacterial components, when used in the formulation of liposomes can enhance the effectiveness of liposomes as delivery systems in the treatment of disease. In this manner, multi-functional liposomes can be developed to treat target diseases. In addn. to serving as antibiotic delivery systems, such liposomes also have an immunization effect. Thus, the liposomes can be used for both the prevention and treatment of diseases. Liposome were prepd. by dissolving in 2:1 chloroform:methanol the lipids phosphatidylcholine:cholesterol:phosphatidylserine in a molar ration of 7:2:1 and the lipid soln. was dried. Then 40 .mu.L of a soln. of smooth lipopolysaccharides (10 mg/mL) from Brucella melitensis was added to the above lipid mixt. followed by addn. of 2 mL of 20 mg/L ciprofloxacin and heated at 45.degree. while vortexing for 15-25 times. The lipid-antibiotic-lipopolysaccharide mixt. was sonicated and freeze-dried to obtain the liposomes of the invention. The protection of mice given multiple doses of above liposomes before infection with B. melitensis were studied.

L54 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
1997:483480 Document No. 127:140433 Degradation and Release Behavior of Dextran-Based Hydrogels. van Dijk-Wolthuis, W. N. E.; Hoogeboom, J. A. M.; van Steenbergen, M. J.; **Tsang, S. K. Y.**; Hennink, W. E. (Department of Pharmaceutics Faculty of Pharmacy Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, 3508 TB, Neth.). Macromolecules, 30(16), 4639-4645 (English) 1997. CODEN: MAMOBX. ISSN: 0024-9297. Publisher: American Chemical Society.

AB Dextran hydrogels were prepd. by radical polymn. of aq. solns. of glycidyl methacrylate-derivatized dextran (dex-MA), hydroxyethyl methacrylate-derivatized dextran (dex-HEMA), and HEMA-oligolactate-derivatized dextran (dex-(lactate)HEMA), using potassium peroxydisulfate and N,N,N',N'-tetramethylethylenediamine (TEMED) as the initiating system. Dex-MA hydrogels only degraded under extreme conditions (100.degree., pH 1-3), whereas hydrogels derived from dex-HEMA or dex-(lactate)HEMA degraded fully at pH 7.2 and 37.degree., due to hydrolysis of the lactate and/or carbonate esters in the crosslinks. The degrdn. time of these gels

can be tailored from 2 days to more than 2 mo by varying the nature of the
spacer, the degree of substitution of dextran (DS), and the initial water content of the hydrogels. The release kinetics of a model **protein**, IgG, from dex-(lactate)HEMA hydrogels were investigated and shown to be dependent on both the DS and the initial water content of the gel. Under certain conditions zero-order release was obsd. over a period of 10 days.

L54 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2001 ACS
1997:230073 Measurement and control of interaction forces between model membrane surfaces and **drug-delivery** systems.
Israelachvili, Jacob; **Wong, Joyce**; Kuhl, Tonya (Dept Chemical Engineering, University California, Santa Barbara, CA, 93106, USA). Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17, BIOC-008. American Chemical Society: Washington, D. C. (English) 1997. CODEN: 64AOAA.
AB A brief review will be given of the major forces that govern the interactions between vesicles, liposomes and cell-membrane surfaces, and why they are much more complex than the forces that act between inert colloidal particle surfaces. We have used a Surface Forces App. to directly measure these forces between surfaces composed of lipid bilayers, surface polymer groups, receptor **proteins** and ligand mols., all of which are involved in the interactions that det. the efficacy of **drug-delivery** systems. Our results reveal the complexity of the overall interaction when non-specific (colloidal type) forces and specific (ligand-receptor type) binding forces act together, and how different forces govern the interaction at different time-scales and distance regimes (which in turn may also be different for approaching and sepg. surfaces).

L54 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2001 ACS
1996:413163 Direct determination of molecular level interactions between surface-bound **protein** receptors and tethered ligands.
Wong, Joyce Y.; Kuhl, Tonya L.; Zalipsky, Samuel; Mullah, Nasreen (Department Chemical Engineering, University California, Santa Barbara, CA, 93106-5080, USA). Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29, COLL-007. American Chemical Society: Washington, D. C. (English) 1996. CODEN: 63BFAF.
AB The well-known property of polyethylene glycol (PEG) to mask the immunogenicity of foreign **proteins** and artificial surfaces has led to large efforts to develop biomaterials and **drug delivery** vehicles which contain PEG on the outer surface. While this has greatly increased the biocompatibility and circulation times in vivo, the next step has been to achieve specific targeting by attaching ligands to the PEG terminus. We have studied the interactions between ligands attached to the end of polyethylene glycol and its corresponding receptor. Using the surface forces app. technique, we were able to investigate the force-distance profile and adhesion at the mol. level. The interaction forces and adhesion were qual. similar to previous studies in which the ligand was directly attached to the surface, but we found that the addn. of the polymer resulted in recognition from a much greater sepn. distance. These results also agree well with independent studies examg. in vitro binding of Stealth liposomes with incorporated targeting

moieties.

L54 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
1995:947089 Document No. 123:350317 Pulmonary **drug delivery** system. **Wong, Jeffrey T. F.**; Tam, Michael S .C. (Hong Kong University of Science and Technology, Hong Kong). U.S. US 5451569 A 19950919, 8 pp. (English). CODEN: USXXAM. APPLICATION: US 1994-229600 19940419.

AB The present invention provides a method of improving the efficiency of absorption into the bloodstream of **drugs delivered** through the pulmonary route. The drug is mixed with surfactant, preferably a surfactant naturally produced by the lung. This method is found to enhance the absorption of pharmaceutical compns., and in particular those comprising **protein**, e.g. insulin, or peptides, e.g. vasopressin. Insulin 40 .mu.L (200 units/mL) was mixed with 60 .mu.L of lung surfactant (40 mg/mL) and the mixt. was administered to rats by the tracheal route and blood glucose levels against time were monitored; the surfactant increased the hypoglycemic effect of tracheally administered insulin.

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=> s (l1 or asialoglycoprotein? receptor? or l2 or desialyated glycoprotein?)
L55          966 FILE MEDLINE
L56        36527 FILE CAPLUS
L57          990 FILE BIOSIS
L58          796 FILE EMBASE

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'GLYCOPROTEINS, SPECIFIC OR
CLASS (L) ASIALOGLYCOPROTE/CT'
L59           38 FILE WPIDS
L60          123 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L61        39440 (L1 OR ASIALOGLYCOPROTEIN? RECEPTOR? OR L2 OR DESIALYATED
GLYCOP
               ROTEIN?)

=> s l61 and (l3 or target? deliver? or therap? agent? or polynucleotide or
cdna or protein or ribozyme or antisense dna or cytotoxic or protein or
doxorubicin or daunorubicin or amphiphat? amine or l4)
L62          479 FILE MEDLINE
L63        24869 FILE CAPLUS
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L64          417 FILE BIOSIS
L65          427 FILE EMBASE
L66           27 FILE WPIDS
L67           85 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L68       26304 L61 AND (L3 OR TARGET? DELIVER? OR THERAP? AGENT? OR
POLYNUCLEOT
                IDE OR CDNA OR PROTEIN OR RIBOZYME OR ANTISENSE DNA OR
CYTOTOXIC
                 OR PROTEIN OR DOXORUBICIN OR DAUNORUBICIN OR AMPHIPHAT? AMINE
                OR L4)

=> s l68 and (avidin(a)biotin or thiol(a)maleamide?)
L69           1 FILE MEDLINE
L70          42 FILE CAPLUS
L71           1 FILE BIOSIS
L72           1 FILE EMBASE
L73           0 FILE WPIDS
L74           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L75          45 L68 AND (AVIDIN(A) BIOTIN OR THIOL(A) MALEAMIDE?)

=> s l75 and (liver or pulmonar? or hepat?)
L76           1 FILE MEDLINE
L77           7 FILE CAPLUS
L78           1 FILE BIOSIS
L79           1 FILE EMBASE
L80           0 FILE WPIDS
L81           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L82          10 L75 AND (LIVER OR PULMONAR? OR HEPAT?)

=> s l75 and (liver or  hepat?)
L83           1 FILE MEDLINE
L84           7 FILE CAPLUS
L85           1 FILE BIOSIS
L86           1 FILE EMBASE
L87           0 FILE WPIDS
L88           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L89          10 L75 AND (LIVER OR HEPAT?)

=> dup rem l89
PROCESSING COMPLETED FOR L89
L90           8 DUP REM L89 (2 DUPLICATES REMOVED)

=> d cbib abs 1-8

L90  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2001 ACS
1997:342720   Document No. 127:64507  Two-step pretargeting methods using
     improved biotin-active agent conjugates.  Reno, John M.; Theodore, Louis
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J.; Gustavson, Linda M. (Neorx Corporation, USA). U.S. US 5630996 A 19970520, 80 pp. Cont.-in-part of U.S. Ser. No. 995,381, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1993-122979 19930916. PRIORITY: US 1992-895588 19920609; US 1992-995381 19921223; US 1992-995383
19921223.

AB Methods, compds., compns. and kits that relate to pretargeted delivery of diagnostic and **therapeutic agents** are disclosed. In particular, methods for radio-metal labeling of biotin and for improved radiohalogenation of biotin, as well as related compds., are described. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention enhancing moieties and addnl. methods are discussed. The method comprises (1) administering a 1st conjugate of antibody or fragment
and streptavidin and allowing time for accumulation in target tissue (tumor), and (2) subsequently administering a 2nd biotindase-resistant conjugate of biotin and DOTA deriv. (chelated with radio-metal, e.g. 99mTc
or 186Re). Asialoorosomucoid may be used as clearing agent for maximize targeting (tumor:blood) ratio.

L90 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2001 ACS

1997:121366 Document No. 126:130594 Improved delivery of diagnostic and **therapeutic agents** to a target site. Griffiths, Gary L.; Hansen, Hans J.; Govindan, Serengulam (Immunomedics, Inc., USA). PCT Int. Appl. WO 9640245 A1 19961219, 41 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US8696 19960607. PRIORITY: US 1995-486166 19950607.

AB An in vivo method for delivering a diagnostic or **therapeutic agent** to a target site in a mammal, wherein a targeting species including a targeting moiety and a diagnostic or **therapeutic agent** or a binding site for a subsequently administered diagnostic or **therapeutic agent** conjugate, the targeting moiety having a primary binding site whereby it specifically binds to the target,
is administered and allowed to accrete at the target site, is improved by injecting into the circulatory system of the mammal a clearing agent that binds to the primary binding site of the targeting species, whereby non-localized primary targeting species is cleared from circulation. The method is esp. useful in pretargeting methods because the clearing agent does not remove the primary targeting species or block secondary binding sites of the primary targeting species. Described are prepn. of streptavidin/anti-carcinoembryonic antigen antibody (IMMU-14) conjugate, prepn. of biotin-carborane-dextran conjugate, prepn. of yttrium-90-labeled
p-[5-(biotinamido)pentyl(amino)thioureayl]-2-benzyl-diethylenetriaminepentaacetic acid (BPD), in vivo localization of Y-90-BPD
to pretargeted streptavidin-IMMU-14, localization of biotin-carborane-dextran to pretargeted streptavidin-IgG, delivery of In-111 to tumor xenografts using the invented pretargeting protocol, etc.

L90 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2001 ACS
1996:504894 Document No. 125:218344 Lectin-binding characteristics of glycoproteins of high- and low-metastatic murine HCa cell lines. Liu, Ji-Lin; Yan, Qiu; Zhu, Zheng-Mei (Dep. of Biochem., Dalian Med. Univ., Dalian, 116023, Peop. Rep. China). Shengwu Huaxue Zazhi, 12(3), 317-321 (Chinese) 1996. CODEN: SHZAE4. ISSN: 1000-8543.

AB Two of recently isolated murine **hepatocarcinoma** subclonal cell lines, HCa-F and HCa-P with high- and low-metastatic potential in lymphatic system resp., were adapted in this study. Cellular glycoproteins of the two cells were analyzed for their relationship to metastasis. After sepd. by SDS-PAGE and electroblotted to NC membranes, the total cellular glycoproteins were overlaid by five different biotin labeled lectins (WGA, Con A, PNA, UEA, SBA) and then revealed by the **avidin-biotin** peroxidase complex (ABC) method. No apparent difference of **protein** sepd. by SDS-PAGE could be seen between the two cells. The major lectin-binding glycoproteins of the cells detected are: five of Con A-binding glycoproteins of Mr .apprx.72, 80 .apprx.90, .apprx.104, .apprx.150, .apprx.200 kD which could be blocked by mannose; one of .apprx.150 kD WGA binding glycoprotein blocked by GLcNAc. There were no specific SBA-UEA-or PAN-binding glycoprotein blocked by GLcNAc. There were no specific SBA-UEA- or PAN-binding glycoproteins in these cells. Most of above detected glycoproteins were similar in amt. between the high- and low-cell lines except that the .apprx.72 kD Con A binding-band, which expressed mainly on HCa-P. This difference might be the result of oligosaccharide changes of glycoprotein. Unexpectedly, two "avidin-binding" **proteins** of Mr .apprx. 79 kD and .apprx.130 kD were detectable in total cellular exts., and the amt. of the latter in HCa-f cells was apparently higher than that in HCa-P cells. The results suggested that quant. rather than qual. changes in cell surface are assocd. with the difference in metastatic behavior of murine HCa cells.

L90 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2001 ACS
1994:570586 Document No. 121:170586 Agents for targeted nitric oxide pathway or nitric oxide synthase modulation for therapeutic effect. Axworthy, Donald B. (Neorx Corp., USA). PCT Int. Appl. WO 9416729 A1 19940804, 44 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US894 19940126. PRIORITY: US 1993-10238 19930128.

AB The present invention is directed to targeted agents capable of modulating a nitric oxide pathway or nitric oxide synthase to achieve a therapeutic effect. Some preferred targeted agents include a targeting portion (e.g. an antibody or **protein** complementary to a target cell receptor) capable of delivering the agent to a target site and an effector portion (arginine or analogs or polymers thereof, heme, cytokines, corticosteroids, aminoguanidine, etc.) capable of modulating a nitric oxide pathway or nitric oxide synthase at the target site. The present invention also provides methods of modulating a nitric oxide pathway or nitric oxide synthase to achieve a therapeutic effect in a target cell

population (e.g. vascular smooth muscle cells, corpora cavernosa smooth muscle cells, endothelial cells, brain cells, **liver** cells). The therapeutic objective may be treatment of restenosis, treatment of septic shock, modulation of inflammation, etc.

L90 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2001 ACS
1994:549768 Document No. 121:149768 Detection of insulin-like growth factor binding **protein**-1 in cat implantation sites. Boomsma, Robert A.; Mavrogianis, Patricia A.; Fazleabas, Asgerally T.; Jaffe, Randal C.; Verhage, Harold G. (Department of Biology, Trinity Christian College, Palos Heights, IL, 60463, USA). Biol. Reprod., 51(3), 392-9 (English) 1994. CODEN: BIREBV. ISSN: 0006-3363.
AB This study was undertaken to det. whether insulin-like growth factor binding **protein**-1 (IGFBP-1) was synthesized by the cat uterus and placenta during implantation and pregnancy. Endometrial and placental tissue explants from pregnant, pseudopregnant, and ovariectomized steroid-treated cats were cultured in the presence of 35S-methionine. Culture media **proteins** were sepd. by one-dimensional (1-D) and two-dimensional (2-D) SDS-PAGE, transferred to nitrocellulose, and immunostained using a rabbit polyclonal antibody against baboon IGFBP-1 and a murine monoclonal antibody to human IGFBP-1. The antibody cross-reacted with a **protein** with an Mr = 30 000 and a pI = 5.1-5.4. Immunoreactive product was found in implantation site media from 16 days postcoitum (PC) through the end of pregnancy, and was confined to the superficial placental/junctional zone. Immunoreactivity was not detected in non-implantation site media until 7 wk PC and was never detected in serum or in media from **liver**, pseudopregnant endometrium, or endometrium from steroid-treated cats. Autoradiog. and immunostaining of 2-D Western blots of culture media **proteins** demonstrated that implantation site and not non-implantation site tissue synthesized and released immunoreactive IGFBP-1 into the culture medium. 125Insulin-like growth factor-I (IGF-I) specifically bound to this **protein** on 1-D Western ligand blots. **Avidin-biotin** immunocytochem. utilizing the monoclonal antibody was used to localize IGFBP-1 in paraffin sections. Specific immunostaining was obsd. in the surface and glandular epithelium of the non-site endometrium throughout pregnancy, with stromal cell staining being detected later. The placental labyrinth had widespread specific immunostaining, esp. in the syncytiotrophoblast and maternal giant cells after 4 wk; after 9 wk, immunostaining could be detected only in the giant cells. All cells in the junctional zone and the deep glandular region of the implantation site contained IGFBP-1 staining. The synthesis of IGFBP-1 and its release into culture medium appears to be dependent on the process of implantation in the cat and may play an autocrine-paracrine role in the control of trophoblast growth and invasion.

L90 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2001 ACS
1994:503458 Document No. 121:103458 Production and characterization of monoclonal and polyclonal antibodies to human .alpha.2-HS: development of a two-site ELISA test. Akhoundi, C.; Rochet, N.; Ferrua, B.; Rossi, B. (U

364 INSERM, Faculte de Medecine, Avenue de Valombrose, Nice, 06107/02, Fr.). J. Immunol. Methods, 172(2), 189-96 (English) 1994. CODEN: JIMMBG.
ISSN: 0022-1759.

AB A convenient and sensitive indirect sandwich ELISA test was developed for measuring both 63 kDa human .alpha.2-HS (Heremans Schmid) glycoprotein secreted by human **hepatoma** cell lines and the 59 kDa .alpha.2-HS species present in serum/plasma. Monoclonal and rabbit antibodies to plasma .alpha.2-HS were produced and selected by immunopptn. techniques using iodinated .alpha.2-HS or 35S-labeled .alpha.2-HS. Various monoclonal antibodies recognizing both forms of the **protein** were coated onto microtiter plates and after binding of .alpha.2-HS, biotinylated monoclonal antibodies with compatible binding or biotinylated immunopurified F(ab')2 fragments from the rabbit antiserum were added and subsequently revealed with **avidin-biotin** peroxidase complex. Formats using a rabbit detector antibody were the most sensitive and one was selected for the whole study. The test developed was capable of detecting plasma .alpha.2-HS devoid of connecting peptide and HepG2 **hepatoma** cell line derived .alpha.2-HS at the ng/mL level. The test has been used to measure levels of .alpha.2-HS in both serum and supernatants from HepG2 cell lines.

L90 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2001 ACS
1993:247616 Document No. 118:247616 Drug delivery of antisense oligonucleotides and peptides to tissues in vivo and to cells using **avidin-biotin** technology. Pardridge, William M.; Boado, Ruben J. (University of California, USA). PCT Int. Appl. WO 9222332 A2 19921223, 43 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US5085 19920617. PRIORITY: US 1991-716062 19910617.

AB A compn. is disclosed for delivery of an agent to cells in vitro or to tissues or organs in vivo. The compn. comprises avidin (or an avidin fusion **protein**) bound to a biotinylated agent to form an **avidin-biotin**-agent complex. A method is disclosed for delivery of an agent to cells using the **avidin-biotin** -agent complex. The complex is useful in diagnostic and therapeutic methods. Biotinylated peptide DDLVP (a vasopressin analog) was taken up by brain capillary prepns. when coupled to avidin, whereas minimal uptake was obsd. without the avidin transport vector. Uptake was mediated by the cationic nature of the avidin rather than the attached carbohydrate. Uptake of an avidin complex with a biotinylated antisense oligonucleotide (complementary to GLUT-1 glucose transporter mRNA) is also described. Further described are the protection by avidin of biotinylated antisense oligonucleotide against degrdn. by serum exonuclease and the facilitation of uptake of biotin by a cationized rat albumin-avidin conjugate.

L90 ANSWER 8 OF 8 MEDLINE DUPLICATE 1
90185573 Document Number: 90185573. PubMed ID: 2312054. Antibodies against the **hepatic asialoglycoprotein receptor** perfused in situ preferentially attach to periportal

liver cells in the rat. McFarlane B M; Sipos J; Gove C D; McFarlane I G; Williams R. (Liver Unit, King's College Hospital, London, U.K.) HEPATOLOGY, (1990 Mar) 11 (3) 408-15. Journal code: GBZ; 8302946. ISSN: 0270-9139. Pub. country: United States. Language: English.

AB Autoantibodies reacting with the galactose-specific **hepatic asialoglycoprotein receptor**--a **liver**-specific component expressed on the surfaces of **hepatocytes**--are often found in patients with chronic active **hepatitis** of presumed autoimmune origin. As part of an investigation into whether these anti-**asialoglycoprotein receptor** antibodies might be involved in the development of periportal **liver** damage in chronic active **hepatitis**, **livers** of ether-anesthetized rats were perfused in situ with polyclonal guinea pig anti-rabbit **asialoglycoprotein receptor** or murine monoclonal anti-human galactose-specific **hepatic asialoglycoprotein receptor** antibodies in excess at less than 8 degrees C or, as a control, with guinea pig anti-human plasma **protein** antibodies or normal guinea pig serum. Rapid (1 min) antegrade (by way of portal vein) or retrograde (through **hepatic** veins by way of vena cava) perfusions were performed in a nonrecirculating (once-through) mode in Ca+(+)-free medium. Blocks of **liver** tissue were immediately snap-frozen and the distribution of the antibody examined in cryostat sections by using an **avidin-biotin** immunohistochemical technique. In all of the perfusions with anti-**asialoglycoprotein receptor** (six antegrade, seven retrograde), the antibodies were found to be prominently and almost exclusively deposited on **liver** cells in the periportal areas. No deposition of immunoglobulins was detected in **livers** perfused with the control guinea pig sera. The findings suggest that the **asialoglycoprotein receptor** is expressed at high density mainly on cells in zone 1 of the **hepatic** lobule, and this may have implications for the development of periportal **liver** damage in chronic active **hepatitis**.

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